Remarks

Claims 1-6, 8, 11-17 and 19-26 stand rejected under 35 USC § 102(b) as being anticipated by WO 98/26747 ('747 publication). Applicants respectfully traverse. The Examiner states that "the '747 publication teaches a method for achieving superantigen mediated expansion of antigen-specific T cells for cancer treatment/prophylaxis which comprises administering a tumor specific antigen composition, including melanoma specific antigen followed by administration of a superantigen (SEA/SEB) composition at an optimized time interval following said administering of said tumor specific antigen composition to maximize the cellular immune response to said antigen." Applicants disagree with the various foundations upon which the Examiner bases this statement. The office action states that the '747 publication "teaches that the optimal timing between immunization with cancer antigen and further administration of superantigen may be anywhere in the range of from minutes to up about [to] about two weeks. . ." The Examiner cites to pages 19 and 72 of the '747 publication in support of this statement. With all due respect to the Patent Office, the '747 publication does not teach this. Page 19 of the '747 publication states that "[W]hen the superantigens and immunotherapeutic antigens are administered separately, the time between administrations may be anywhere in the range of from a few minutes to up to about one week. ..."(emphasis added). Clearly, the teaching on page 19 limits the time in which superantigen should be administered to 7 days or less. The Examiner seems then to be relying on the language at page 72 that "[T]he optimal timing of superantigen introduction after peptide stimulation is between 3 and 14 days." However, this is improper because this statement strictly relates to a protocol of achieving clonal expansion of T cells *in vitro*; it has nothing to do with *in vivo* immunization. The Patent Office should not confuse one straightforward teaching by the '747 Publication to mean something that is not taught by the '747 Publication in order to support a claim rejection. Certainly the Patent Office must agree that a cell expansion protocol carried out *in vitro*, much less an *in vitro* protocol utilizing an unrelated antigen, does not anticipate an *in vivo* administration regimen shown to prevent the onset of melanoma.

Next, the Examiner cites to pages 7, 8 and 77 for the proposition that the '747 publication teaches that "the method of the ['747 publication] invention can be used to induced [sic] T cellular immune response, not anergy for cancer treatment, including melanoma development." First, the Applicants wish to point out the distinction between a immunotherapy and prevention, which will be discussed below. With respect to pages 7 and 8, the '747 publication merely discusses, in very generic terms, what immunotherapeutic antigens are. They teach that an immunotherapeutic antigen is one that binds to a T cell receptor of a lymphocyte population that would either stimulate such lymphocyte population or anergize it. See last paragraph on page 7. This is merely a statement of a well known definition. However, page 9 sheds further light on the context of the '747 publication's intended use of such immunotherapeutic agents. "The invention provides methods and compositions for enhancing the *in vitro* stimulation by utilizing superantigens in conjuction with immunotherapeutic antigens (line 1, page 9, '747 publication). Again, the '747 publication is teaching the *in vitro* not *in vivo* use of an immunotherapeutic agent. This is further underscored on page 77, which the Examiner cites. Page 77 indisputably is devoted to techniques for stimulating T cells in vitro. The Applicants respectfully ask the Examiner to carefully review page 77, and if in disagreement with the Applicant's position concerning page 77, please provide specific reasoning, with cites, that the '747 publication does not teach only the *in vitro* stimulation of T Cells. Indeed, Applicant's particularly note that page 77 of the '747 publication does not even teach sequential administration of an antigen followed by a superantigen for its *in vitro* stimulation of T cells. In sum, pages 7, 8 and 77 fail to teach an *in vivo* administration regimen that involves the *in vivo* administration of an antigen followed by the *in vivo* administration of a superantigen at an optimized time interval thereafter.

The Examiner next cites to page 69 of the '747 publication for the assertion that the '747 publication teaches the use of its method to prevent the onset of tumor development. This proposition is debatable on its face, since the method that the Examiner cites to involves the removal of tumor cells from the patient (paragraph A, page 69). Nonetheless, page 69 does not teach the *in vivo* administration of a melanoma specific antigen followed by *in vivo* administration of a superantigen composition. Page

69 teaches the removal of autologous tumor cells from a patient for subsequent isolation and stimulation *in vitro*.

With respect to any disclosure in the '747 publication that could be characterized as pertaining to an in vivo administration strategy, the '747 publication emphasizes that the delay between antigen administration and superantigen administration should be no more than 6-7 days. At the bottom of pages 78 of the '747 Publication, there is a section entitled "Does Variations of Peptides and/or Superantigens to Product Energy or Sensitization of Effector T Cells for Autoimmune, Neoplastic or Infectious Disease." On the next page, page 79, still under this same section, the paragraph beginning with "*in vivo* immunizing schedules ...," the '747 Publication teaches that anergy is avoided by co-administering the antigen with the superantigen. Then, keeping in mind the objective to achieve anergy, in the same paragraph, the '747 Publication teaches that "anergy may be produced by preimmunization with peptide in solution followed within six to thirty days by superantigen given parenterally" (emphasis added). Accordingly, the '747 publication teaches that to induce an immune response and avoid anergy, superantigen should be administered six days or earlier from administration of antigen. By following the teachings of the '747 Publication to avoid anergy, administration of a superantigen ideally is delayed at least seven days after administration of an antigen. Indeed, the closest teaching in the '747 Publication of producing an immune response to treat a disease notes that the delay in administering a superantigen after administration of an immunotherapeutic antigen is no more than six days. Conversely, the '747 Publication teaches that anergy can be achieved by delay of administration of a superantigen six days or more after administration of an antigen. Thus, the '747 Publication wholly misses the importance of the delay of the administration of a superantigen to achieve the desired prophylactic immune response, which is the primary objective of the subject application.

In view of the foregoing remarks, Applicants respectfully assert that the '747 publication does not teach all of the elements of claims 1-6, 8, 11-17 and 19-26. Reconsideration and withdrawal of the 35 USC § 102(b) rejection is respectfully requested.

Claims 15, 9, 11, and 14-17 are rejected as being anticipated, and/or obvious over, the Kominsky et al. references. In reviewing these references, the inventors became aware that an inventor may have been inadvertently omitted from the subject application. Therefore, this matter is being resolved and a petition under 37 CFR 1.48 requesting change in inventorship, if necessary, will be forthcoming. This petition will be accompanied by a Declaration of Dr. Johnson which will establish that the work provided in the Kominsky et al. references represents work derived from himself and the other inventors of the present application, as corrected. Alternatively, no petition will be filed and only a Declaration of Dr. Johnson establishing that the work in the Kominsky et al references represents the work of the currently named inventors will be filed. These documents will follow this response and should be received by the USPTO in ample time for the Examiner to review concurrently with this response. Reconsideration is requested.

Lastly, the Patent Office rejects claims 1-6, 8 and 11 under 35 USC § 112, first paragraph, as the phrase "prior to melanoma development" previously added to claim 1 is said to pertain to new subject matter. Applicants respectfully traverse. Applicants recognize that the exact wording "prior to melanoma development" was not originally provided in the application as filed, but assert that it is logical and legitimate rephrasing of language in the application as filed. Examples 10-12 of the application teach that a vaccination treatment comprising the administration of an antigen followed by the administration of a superantigen. This treatment is performed prior to challenge to melanoma. Claim 12 as originally filed claimed a "method of protecting an animal or human against infection and tumor development..." It is only logical that protection against tumor development pertains to treatment prior to tumor development. Thus, a method that involves a treatment step prior to melanoma development is implicit in the teachings of the application as filed. Applicants remind the Examiner that the subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. M.P.E.P. 2163.02. A rewording of a passage where the same meaning remains intact is

permissible. *In re Anderson*, 471 F.2d 1237, 176 USPQ 331 (CCPA 1973). Mere rephrasing of a passage does not constitute new matter. M.P.E.P. 2163.07. Because the phrase "prior to melanoma development" is described logically and implicitly in the application as filed, Applicants respectfully request reconsideration and withdrawal of this 35 USC § 112, first paragraph rejection.

Applicants assert that all pending claims are in a condition for allowance, and indication of this requested in the ensuing office action. Applicants invite the Examiner to call the undersigned if clarification is needed on any aspect of this response after entrance and consideration of the remarks presented herein.

Respectfully submitted,

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